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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ROBINS & PASTERNAK 1731 EMBARCADERO ROAD SUITE 230 PALO ALTO, CA 94303			LAMBERTSON, DAVID A	
			ART UNIT	PAPER NUMBER
			1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/888,049

Applicant(s)

FRANCIS ET AL.

Examiner

David A. Lambertson

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 July 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) ☐ they raise the issue of new matter (see Note below);
 - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☒ Applicant's reply has overcome the following rejection(s): see continuation sheet.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see continuation sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____

Claim(s) objected to: 19-22,24-42,45,46 and 59.Claim(s) rejected: 1-3,5-18,23,47-52 and 58.Claim(s) withdrawn from consideration: 43,44 and 53-57.

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
10. ☒ Other: see continuation sheet

ADVISORY ACTION

This is a continuation sheet for the form PTOL-303.

3. Applicant's reply has overcome the following rejection(s): 35 USC § 102(b) with regard to Knudtson. It is noted that this rejection is overcome by the amendment of claim 1 to contain the limitations set forth in claim 4. Because Knudtson does not anticipate the limitation, the rejection is obviated as it regards 35 USC § 102(b) only. However, the merits of the reference still apply to the rejections under 35 USC § 103(a). Thus, the traversal of Knudtson as a reference will be addressed below in response to the traversal of the rejections under 35 USC § 103(a), set forth in section 5.

5. The c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: the following rejections are maintained under 35 USC § 103(a) in view of Applicant's amendment and traversal:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 5, 13-15, 23, 47, 50-52 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knudtson in view of Lajoie as set forth in the previous Office actions.

Although it is noted that this rejection is identical to the previous rejection because all of the above claims were included in the previous rejection (see page 7 of the Final Office

Action), this rejection is necessitated by the amendment of claim 1 to contain the limitation of claim 4.

Claims 6-10, 16, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knudtson in view of Lajoie (as applied to claims 1-3, 5, 13-15, 23, 47, 50-52 and 58), and in further view of Jacobs, as set forth in the previous Office Actions. **It is noted that this rejection is identical to the previous rejection because all of the above claims were included in the previous rejection (see page 8 of the Final Office Action).**

Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knudtson and Lajoie in view of Jacobs (as applied to claims 1-3, 5-10, 13-16, 23, 47-52 and 58), and in further view of Baldwin, as set forth in the previous Office Actions. **It is noted that this rejection is identical to the previous rejection because all of the above claims were included in the previous rejection (see page 8 of the Final Office Action).**

Claims 17, 18 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knudtson and Lajoie in view of Jacobs (as applied to claims 1-3, 5-10, 13-16, 23, 47-52 and 58), in further view of Baldwin, as set forth in the previous Office Action. **It is noted that this rejection is identical to the previous rejection because all of the above claims were included in the previous rejection (see page 8 of the Final Office Action).**

Applicant's arguments filed July 15, 2004 have been fully considered but they are not persuasive. The following grounds of traversal are supplied:

1. It is asserted that The Office has ignored functional limitations in the claims that define the invention. Specifically, it is asserted that Knudtson fails to teach that the transposon cassette is capable of promoting the expression of a gene of interest in a gram-positive organism. It is further alleged that the Office has dismissed this limitation as irrelevant (see for example pages 13-14 of Applicant's response, the section regarding 35 USC § 102(b)). It is additionally asserted that the target organism is entirely relevant, and that there is nothing improper in the claim (see for example pages 15-16, the bridging paragraph of Applicant's response).
2. It is asserted that there is no motivation to combine the references set forth in the previous Office Actions (see for example page 14, fourth full paragraph of Applicant's response), and that there is no teaching that the claimed invention is desirable (see for example page 15, second full paragraph of Applicant's response).
3. It is asserted that the Office has used impermissible hindsight to reconstruct the invention as claimed (see for example pages 14-15 of Applicant's response, the bridging paragraph).
4. It is further suggested that Knudtson is "entirely silent as to both light generating proteins and gram-positive bacteria," coupled with the lack of a teaching in Lajoie concerning gram-positive bacteria, it is asserted that the combined teachings do not meet the limitations of the claimed invention (see for example page 15, third full paragraph of Applicant's traversal).
5. It is argued that Jacobs uses a promoter, and that this teaches away from the promoterless cassettes of the instant invention (see for example page 15, fourth full paragraph).

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Applicant's arguments are not found convincing for the following reasons:

1. The contention of the argument is that Knudtson does not teach a transposon cassette that would be functional in gram-positive bacteria simply because Knudtson does not use their transposon cassette in a gram-positive bacterium. Thus, the argument is based upon an intended use of the claimed transposon cassette, and not the transposon cassette itself.

It is an erroneous assertion that the Office dismisses the ability of the transposon cassette to function in a gram-positive organism as irrelevant. Rather, the Office asserts that the argument that the Knudtson reference does not use their plasmid in a gram-positive bacterium is irrelevant. The Office acknowledges the requirement that the transposon cassette be functional in gram-positive bacteria, and provides evidence as to why the cassette taught by Knudtson meets these functional limitations; specifically, the cassette uses transposon sequences originating from a transposon that is functional in gram-positive bacteria. Applicant asserts that, because Knudtson does not use their transposon cassette in a gram-positive organism, the Knudtson cassette would not be functional in a gram-positive organism. This argument is similar to claiming aspirin, wherein the aspirin is functionally capable of treating heart disease. The fact that aspirin was taught in the art as a treatment for pain symptoms does not make that same aspirin non-functional with regard to treating heart disease. Thus, where Knudtson chooses to use their cassette does not impede its functionality in other organisms; it is again asserted that where Knudtson teaches using the cassette is irrelevant, so long as Knudtson still meets the functional requirements of the claim, which it does as evidenced below and in the previous Office Actions.

The transposon cassette taught by Knudtson meets the structural limitations of the claimed invention (there being no arguments as to what structural element is missing from the teachings of Knudtson), which was clearly set forth in the previous Office Action; therefore Knudtson necessarily teaches the transposon cassette as claimed. Furthermore, the previous Office Action clearly indicates that the transposon elements used by Knudtson (i.e., the transposon sequences of TN40001) originate from and are functional in *S. aureus*, which is a gram-positive organism. In order to meet the functional limitation of the claims, a transposon cassette need only be capable of inserting into the genome of a host cell. Since the sequences responsible for this function in Knudtson (the TN4001) originate from a gram-positive organism, these sequences are functional in a gram-positive organism, absent evidence to the contrary that TN4001 will not function in a gram-positive organism. In summation, because Knudtson teaches a transposon cassette that has sequences from a transposon that is functional in a gram-positive organism, Knudtson necessarily teaches a transposon cassette that is functional in a gram-positive organism, contrary to Applicant's assertion that it does not.

It is noted that Applicant provides no arguments regarding the origin of the transposon elements in Knudtson, and does not dispute that these elements would be functional in a gram-positive bacteria. Again, Applicant merely asserts that because Knudtson does not specifically use their cassette in a gram-positive organism, the cassettes would not be functional in a gram-positive organism. However, this argument does not consider that the structural and functional limitations of the claimed product are met by the teachings of Knudtson. Thus, the argument that the transposon cassette taught by Knudtson is not functional in gram-positive organisms is not convincing, absent evidence to the contrary.

2. The previous Office Actions provide clear motivation to combine the teachings of Knudtson and Lajoie, that being that the lux genes are *preferred reporter genes* (see for example pages 6-7, bridging paragraph of the Office Action mailed November 26, 2003), and it is obviously desirable to use a preferred reporter. Clear motivation is also provided for combining Knudtson and Lajoie with Jacobs (see page 8, first full paragraph of the Office Action mailed November 26, 2003), Knudtson, Lajoie and Jacobs with Baldwin (see page 9, third full paragraph of the Office Action mailed November 26, 2003), and Knudtson, Lajoie and Jacobs with Wagner (see page 10, third full paragraph of the Office Action mailed November 26, 2003). Because Applicant has not specifically pointed out what is improper regarding the motivations to combine for each reference, the arguments cannot be addressed any further.
3. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).
4. As set forth above, Knudtson is not silent with respect to gram-positive bacteria, as asserted by Applicant. The transposon elements used in the cassette as taught by Knudtson originate from TN4001, a transposon that is *functional* in gram-positive bacteria. As set forth above, these sequences are *functional* in gram-positive for that very same reason. While Knudtson is silent with regard to the use of a light generating protein, it does make use of the lacZ reporter gene.

Lajoie teaches that the lux gene is a preferred substitute for lacZ as a reporter gene, and this is clearly set forth in the previous Office Actions (see for example pages 6-7 of the Office Action mailed November 26, 2003). In the rejection, the Office clearly sets forth adequate motivation and obviousness for combining the references, and no evidence to the contrary is provided regarding an expectation of success. Thus, it is maintained that the combined teachings of Knudtson and Lajoie teach the invention as claimed.

5. The fact that Jacobs teaches the use of a promoter does not teach away from the combination of Jacobs with Knudtson and Lajoie. The premise of the Knudtson and Lajoie references is the use of the lux reporter gene in a transposon cassette to identify promoters following insertion of the transposable element into a host cell genome. Jacobs teaches that the use of the ribosome-binding site (RBS) enhances the expression of lux genes from any promoter. The ordinary skilled artisan would recognize that the RBS would be extremely desirable in the promoterless cassettes of Knudtson and Lajoie, and would further recognize the absurdity of including the promoter of Jacobs in a promoterless transposon cassette. There is nothing in Jacobs that teaches the RBS only functions with their particular promoter; rather, the ordinary skilled artisan would recognize that the RBS will work in conjunction with virtually any promoter, including one that is located in a host cell genome. Thus, because Jacobs does not teach that the RBS element would be non-functional in a promoterless cassette used to identify native promoters in a host cell, Jacobs does not teach away from the Knudtson and Lajoie. As such, the rejection is maintained as proper.

In conclusion, Applicant's traversal is not convincing. Knudtson does indeed teach a transposon cassette that would be functional in a gram-positive organism by virtue of the fact

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that it uses transposon sequence elements from TN4001, a transposon that originates from and is functional in a gram-positive organism. Knudtson teaches all of the structural elements of the claimed invention, and these sequences will permit insertion into a gram-positive host cell.

Applicant's only argument is that Knudtson does not actually use their invention in a gram-positive host cell; this is an argument of *intended use of a product claim*, and does not change the fact that the product taught by Knudtson meets the structural and functional limitations of the claimed invention. Furthermore, there is adequate motivation provided by the Office for combining each of the cited references, none of which are specifically traversed in Applicant's responses. As such, the rejections set forth above and in previous Office Actions are maintained.

10. Other: Applicant continues to traverse the restriction requirement. The following reasons are provided:

1. The difference between "commensurate" and "overlapping" is irrelevant to the Restriction requirement. What is relevant is the search burden on the Office, and this has nothing to do with "commensurate" and "overlapping."
2. It is asserted that each of the inventions is classified in the same class, and thus can be searched simultaneously.

The traversal is not convincing for the following reasons:

1. The difference between "commensurate" and "overlapping" is indeed relevant to the Restriction requirement. Because "commensurate" and "overlapping" are distinct, and because the instant inventions are overlapping and not commensurate, there is a search burden associated with subject matter that is "overlapping." As presented in the Office Action mailed November


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26, 2003, "overlapping" subject matter does not necessarily produce prior art that concerns either or both inventions. Specifically, the Office presented that "To be overlapping is insufficient because an art search may turn up art on one invention in a portion that is not overlapping with the other invention, and vice versa. In order to ensure that the full scope of the claims is searched, the Office would have to perform distinct searches when two inventions that merely overlap are concerned, in order to ensure a search of the areas that do not overlap. The Office cannot simply search the area that is shared between the inventions because there may be art on one or both of the inventions in the non-overlapping areas" (see the previous Office Action mailed May 18, 2004). Thus, because the Office would have to perform multiple distinct searches, there is a clear search burden. This is supported by the distinct classification of each group.

2. Applicant's argument that all of the groups are classified similarly is not accurate; a proper classification includes the subclasses of a group. Thus, the classifications of the instant groups are: 435/320.1, 435/473, 435/4, 435/455, 435/7.95 and 435/29. These represent six different classifications, requiring six different searches. Because multiple searches are required to search each of the inventions, said searches would be burdensome.

As indicated previously, the restriction requirement is deemed proper, and is maintained.

This application contains claims 43, 44 and 53-57, drawn to an invention nonelected with traverse in the reply filed on September 2, 2003. A complete reply must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.



JAMES KETTER
PRIMARY EXAMINER